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Hoofbeats and Zebras: Neurodegenerative disorder presenting as a 'first-episode' of psychosis

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Abstract

Neurodegenerative disorders can include diverse neuropsychiatric symptoms. Here we present a case referred to a 'first-episode' psychosis clinic with socio-occupational decline, auditory hallucinations and paranoid ideation who subsequently exhibited a rapid, severe cognitive and behavioral decline. The brain MRI findings of the patient have shown a progressive cortical atrophy prominent in the frontal lobes, due to a neurodegenerative disorder.

Introduction

Neurodegenerative disorders, such as Frontotemporal Dementia (FTD), may present without neurologic symptoms. Its clinical presentation includes changes in behavior and personality with an earlier age of onset than other dementias [1]. The initiation of the illness mimics psychotic disorders [2]. Even though delusions and hallucinations are uncommon manifestations, they occur [3]. Distinguishing FTD from psychosis is possible with a detailed clinical evaluation of the behavioral features [4,5] The gold standard for diagnosis involves examining biopsy specimens from affected brain tissue [6,7,8]. Neuropathologic findings are also heterogenous [9]. Long-term observation, further neuropsychological and radiologic examination may increase the accuracy of diagnosis [4].

CASE REPORT

FN is a 33 year-old female with hypertension and sickle cell anemia trait. She was admitted for her first inpatient psychiatric hospitalization with a new onset psychosis of unclear etiology.

One year prior she had seen a psychiatrist for affective lability and crying spells without psychotic symptoms after the birth of her second child and was treated with sertraline and low dose risperidone. She discontinued medications within few weeks. Afterward she gradually started having difficulties caring for her children, functioning at work due to symptoms such as disorganization, uncontrolled crying, and delusions of persecution and passive suicidal ideation. Except the brief treatment with sertraline and risperidone she did not get any treatment until the hospitalization. She does not have a history of past psychiatric disorder including substance abuse nor a family history of mental illness.

At her first admission she was presented with disorganized behavior (going to the bathroom repeatedly, wandering away), auditory hallucination (her sister's voice) and multiple somatic complaints (blurred vision, lightheadedness, chest pain). The auditory hallucinations resolved with fluphenazine 5 mg/day. The investigations could not confirm any physiological cause for the somatic symptoms. After 24 days, she was discharged with the diagnosis of schizoaffective disorder, on fluphenazine and cogentin. One week after discharge she was re-admitted with worsening disorganization. She was transitioned to clozapine, which titrated to a dose of 600 mg/day, without significant improvement after 8 weeks. Clozapine level of 1400ng/ml (reference levels 350–420 ng/ml) at 600 mg/day confirmed an adequate trial. Augmentation with 14 sessions of ECT proved ineffective. During the 12 weeks of the second hospitalization she continued to decline showing inappropriate sexual behavior (public masturbation, grabbing). She was unable to dress and eat without being redirected. Neurologic examination was unremarkable except the frontal lobe signs of affective flattening, alogia and anhedonia. Metabolic panel proved non-informative. Structural brain MRI with limited information due to the motion artifact, showed no gross abnormality. MRA was normal excluding vasculitis of CNS. EEG was normal. Neuropsychological testing was limited by her disorganized behavior. She was transferred to a longer stay inpatient unit, where her level of functioning continued to decline. Additional features were hyperorality (oral exploration of inedible objects), flattened affect, and urinary incontinence. Urinary incontinence and flattened affect may be seen due to the side effects of clozapine. However continuity of these symptoms after the cessation of clozapine was considered to be features of FTD. Two years later, she remains as a resident at a skilled nursing facility, which provides a high level of support and frequent redirection. She is prescribed quetiapine 450 mg/day (for psychotic symptoms and agitation), lorazepam prn (for anxiety and difficulty sleeping) and valproate 500 mg/day (for disinhibition). She is uncooperative with a neurologic examination, wanders around the room with crying spells.

Additional testing to rule out infectious etiologies was performed in serum and CSF. The serum levels for spirochete-specific antibodies and HIV antibodies were tested. CSF was tested for protein 14-3-3 (supportive for the diagnosis of CJD), West Nile virus IgM and IgG, HSV DNA PCR and enterovirus RT PCR and sent for viral culture. All results were normal.

Repeat structural brain MRI was performed at two different time points with a 15-month interval. The comparison has shown significant progression of global cortical atrophy prominent in the frontal lobes. (Fig.1a–1b)

Discussion

Her initial presentation of mood lability was treated as depression but failed to respond to medication. Subsequently she continued to have symptoms of new onset psychosis. She was referred to a 'first-episode' psychosis clinic. Her partial response (improvement in auditory

hallucinations) to the first antipsychotic medication with fluphenazine has led the treatment to the second trial with clozapine and ECT augmentation.

However, rapid cognitive and behavioral decline, unresponsive to antipsychotic medications cast doubt on her initial diagnosis. The repeated brain MRI studies have shown the cerebral volume loss prominent in the frontal lobes, which is consistent with the structural MRI findings in patients with FTD. The level of atrophy in these patients varies depending on the stage of the disease [4]. The differential diagnosis of Creutzfeldt-Jakob Disease, CNS Whipple's Disease, Paraneoplastic Cerebellar Degeneration were considered and excluded by relevant test results. Another possible diagnosis was frontotemporal dementia. The patient has shown both the core symptoms (i.e. gradual progression, early decline in social interpersonal conduct, emotional blunting, loss of insight) and the supportive symptoms (i.e. decline in grooming, mental rigidity, distractibility, hyperorality and dietary changes, perseverative and stereotyped behavior and urinary incontinence) of FTD [10,11]. The lack of response to the anti-psychotic treatments and the MRI findings were supportive for the diagnosis of FTD [12] (Figure 1a–1b).

Conclusion

The absence of the effective diagnostic tools and the diversity of the symptoms may cause delay in the diagnosis of the neurodegenerative syndromes such as FTD. Careful clinical evalutions, behavioral rating scales and neuroimaging may assist in the differentiation between FTD and common psychiatric disorders. Earlier diagnostic identification would allow for more proactive case management, including the identification of appropriate housing and nursing resources in the community.

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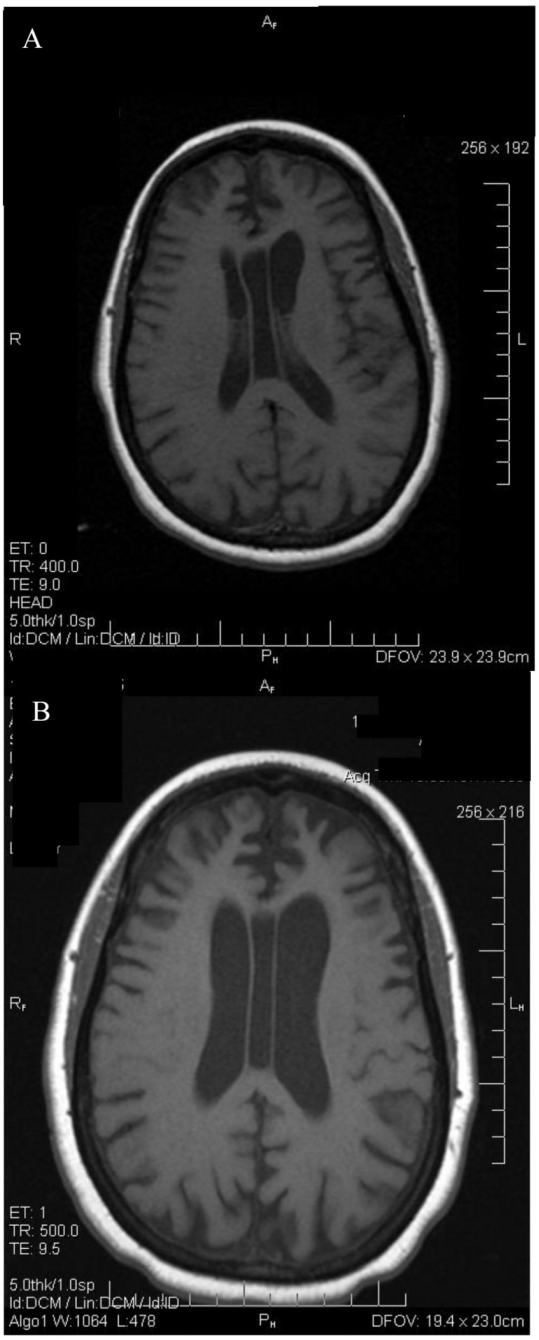

Figure 1.

A, B. An interval of 15 months between two imaging studies (A; the first repeat MRI, B; the second repeat MRI) showed a significant worsening in the cerebral volume loss prominent in the frontal lobes.